



## **DEPARTMENT OF COMMERCE**

### **Bureau of Industry and Security**

#### **15 CFR Part 774**

**[Docket No. 230412-0100]**

**RIN 0694-AI84**

### **Section 1758 Technology Export Controls on Instruments for the Automated Chemical Synthesis of Peptides**

**AGENCY:** Bureau of Industry and Security, Department of Commerce.

**ACTION:** Proposed rule.

**SUMMARY:** The Bureau of Industry and Security (BIS), maintains controls on the export, reexport and transfer (in-country) of dual-use items and less sensitive military items pursuant to the Export Administration Regulations (EAR). Certain instruments for the automated synthesis of peptides (automated peptide synthesizers) have been identified by BIS as a Section 1758 emerging and foundational technology. In this rule, BIS proposes controls for these automated peptide synthesizers. BIS is seeking public comments on the proposed controls, detailed below.

**DATES:** Comments must be received by BIS no later than **[INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER]**.

**ADDRESSES:** You may submit comments, identified by regulations.gov docket number BIS-2022-0023 or by RIN 0694-AI84, through any of the following:

- Federal eRulemaking Portal: <https://www.regulations.gov>. You can find this advance notice of proposed rulemaking by searching for its regulations.gov docket number, which is BIS-2022-0023.

- Email: [PublicComments@bis.doc.gov](mailto:PublicComments@bis.doc.gov). Include RIN 0694-AI84 in the subject line of the message.

All filers using the portal or email should include the name of the person or entity submitting the comments in the name of their file(s), in accordance with the instructions below. Anyone submitting business confidential information should clearly identify the business confidential portion at the time of submission, file a statement justifying nondisclosure and referring to the specific legal authority claimed, and provide a non-confidential submission to be made publicly available.

For comments submitted electronically containing business confidential information, the file name of the business confidential version should begin with the characters “BC.” Any page containing business confidential information must be clearly marked “BUSINESS CONFIDENTIAL” on the top of that page. The corresponding non-confidential version of those comments must be clearly marked “PUBLIC.” The file name of the non-confidential version should begin with the character “P.” The “BC” and “P” should be followed by the name of the person or entity submitting the comments or rebuttal comments. Any submissions with file names that do not begin with a “P” or “BC” will be assumed to be public and will be made publicly available through <https://www.regulations.gov>.

**FOR FURTHER INFORMATION CONTACT:**

For questions on automated peptide synthesizers, contact Dr. Tara Gonzalez, Chemical and Biological Controls Division, Office of Nonproliferation and Treaty Compliance, Bureau of Industry and Security, Telephone: (202) 482-3343, Email: [Tara.Gonzalez@bis.doc.gov](mailto:Tara.Gonzalez@bis.doc.gov).

For questions on the submission of comments, contact Logan Norton, Regulatory Policy

Division, Office of Exporter Services, Bureau of Industry and Security, U.S. Department of Commerce, (202) 482-1762, Email: RPD2@bis.doc.gov.

## **SUPPLEMENTARY INFORMATION:**

### **Background**

#### **Identification of Section 1758 Technologies**

As part of the National Defense Authorization Act (NDAA) for Fiscal Year 2019 (Public Law 115-232), the United States Congress enacted the Export Control Reform Act of 2018 (ECRA) (50 U.S.C. 4801-4852). Section 1758 of ECRA authorizes BIS to establish appropriate controls on the export, reexport or transfer (in-country) of emerging and foundational technologies essential to the national security of the United States. ECRA does not differentiate between the terms “emerging technology” and “foundational technology,” nor does it provide specific definitions or other guidance for these terms. Given this, and to ensure greater efficiency in implementing controls for such items, BIS has chosen to characterize such technologies as “Section 1758 technologies”, rather than characterizing a specific technology as either “emerging” or “foundational.”

As described in section 1758(a)(2)(B) of ECRA, the identification of Section 1758 technologies takes into account: (i) the development of these technologies in foreign countries; (ii) the effect export controls imposed pursuant to this section may have on the development of such technologies in the United States; and (iii) the effectiveness of export controls imposed pursuant to this section on limiting the proliferation of the emerging and foundational technologies in foreign countries.

The Secretary of Commerce must establish appropriate controls on the export, reexport, or transfer (in-country) of technology identified pursuant to the Section 1758 process. In so doing, the Secretary must consider the potential end-uses and end-users of Section 1758 technologies and the countries to which exports from the United States are

restricted (e.g., embargoed countries). While the Secretary has discretion to set the level of export controls, at a minimum a license must be required for the export of such technologies to countries subject to a U.S. embargo, including those countries subject to an arms embargo. Also, section 1758(a)(2)(C) of ECRA requires the interagency process for identifying Section 1758 technologies to include a notice and comment period.

### **November 19, 2018 Advance Notice of Proposed Rulemaking**

On November 19, 2018, BIS published an advance notice of proposed rulemaking (ANPRM), “Review of Controls for Certain Emerging Technologies” (83 FR 58201) (November 19 ANPRM). The November 19 ANPRM identified biotechnology in a representative list of fourteen technology categories concerning which BIS sought public comment to determine whether there are specific emerging technologies that are essential to U.S. national security and for which effective controls can be implemented.

### **September 13, 2022 Advance Notice of Proposed Rulemaking on Instruments for the Automated Chemical Synthesis of Peptides**

On September 13, 2022, BIS published an ANPRM, “Request for Comments Concerning the Imposition of Section 1758 Technology Export Controls on Instruments for the Automated Chemical Synthesis of Peptides” (87 FR 55930) (September 13 ANPRM).

As described in the September 13 ANPRM, peptides and polypeptides are polymeric chains of amino acids, linked together by peptide bonds. Proteins are three-dimensional (3D) macromolecules composed of one or more folded large chains of polypeptides. Proteins must fold into the correct 3D shape to be functionally active.

The first peptide bond was synthesized over 100 years ago; however, in the last few decades advances in chemical synthesis methods have established automated peptide

synthesis as a common laboratory technique.<sup>1</sup> Long-established synthesis methods using fluorenylmethyloxycarbonyl (Fmoc) chemistry can reliably and routinely produce high quality polypeptides around 50 amino acids in length.<sup>2</sup>

Recent advances in peptide synthesis technology and instrumentation have increased both the speed of peptide synthesis and the length of peptide products, including peptides and proteins greater than 100 amino acids in length.<sup>3</sup> Most protein toxins on the Commerce Control List (CCL), which are controlled under ECCN 1C351, are over 100 amino acids in length and have an average length of 300 amino acids, with the notable exception of conotoxins which range between 10-100 amino acids in length.

BIS received five comments in response to the publication of its September 13 ANPRM. The substance of the comments, together with BIS's responses, are detailed below.

*Comment 1:* One commenter stated that synthesis of toxins using automated peptide synthesis is not viable, with the minor exception of conotoxins. The commenter also stated that synthesis of the alpha-conotoxins would not be possible at quantities necessary to cause a significant environmental or terroristic threat.

*BIS Response 1:* BIS concurs that automated peptide synthesizers are currently limited to the production of shorter peptide toxins, including CCL controlled conotoxins. However, BIS believes that the current instrumentation can produce enough peptide toxin to cause mortality and morbidity within a given population.

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<sup>1</sup> R. B. Merrifield, Solid Phase Peptide Synthesis. I. The Synthesis of a Tetrapeptide, 85 J. of the Am. Chem. Soc'y 2149, 2149-54 (1963).

<sup>2</sup> Da'san M. M. Jaradat, Thirteen decades of peptide synthesis: key developments in solid phase peptide synthesis and amide bond formation utilized in peptide ligation, 50 Amino Acids 39, 39-68 (2018); Sameer S. Kulkarni et al., Rapid and efficient protein synthesis through expansion of the native chemical ligation concept, 2 Nature Reviews 1, 1-17 (2018).

<sup>3</sup> Kulkarni, supra note 2, at 1-17.

*Comment 2:* One commenter stated that controlled toxins can be produced manually, and that automation simply speeds up this process. Another commenter stated that export controls for the reagents and consumables could potentially control access to peptide synthesis. However, they further stated that major manufacturers of these items are located outside of the United States.

*BIS Response 2:* BIS appreciates the comments about availability of reagents and consumables for both automated and manual production of peptides. BIS will continue to investigate potential export controls on the consumables for peptide synthesis.

*Comment 3:* One commenter stated that new technological developments for peptide synthesizers aid in making many different types of peptides faster, more efficiently, and at lower cost. They further state that this is primarily useful for research for screening many different peptides for drug candidates.

*BIS Response 3:* BIS concurs with the usefulness of multiplexed automated peptide synthesizers for potential therapeutic development. However, BIS notes that these features can also be useful for other, more dangerous purposes, such as in a weapons program.

*Comment 4:* A common comment was that BIS should not unilaterally control these technologies. A common thread was that these controls could have a dramatic impact on the leadership of U.S. technology in the field as customers would obtain the technology from Europe where it is unrestricted. One commenter noted that the U.S. Government should allow free use by academia to benefit overall development of biomolecular research.

*BIS Response 4:* BIS will work with its international partners to provide multilateral controls for these technologies. However, BIS can take unilateral action regarding these technologies going forward, as necessary. BIS welcomes additional input

on control of these technologies, as indicated and facilitated by this rule's proposed regulatory text.

*Comment 5:* One commenter noted that at this time, the majority of large-scale production of peptides occurs manually.

*BIS Response 5:* While this may be true, and worth looking at for further possible regulatory response, BIS is not inclined to halt the proposal of regulatory text for automated peptide synthesizers. However, BIS notes that this and other related information is relevant to fully understanding the automated peptide synthesizer market and appreciates the information.

### **Proposed Regulatory Changes**

With this rule, BIS proposes changes to ECCN 2B352. The proposed text will create a new item paragraph .k, which will contain three subparagraphs .k.1, .k.2, and .k.3. Item paragraph .k will control peptide synthesizers that are: partly or entirely automated (.k.1), capable of generating continuous peptide sequences greater than 75 amino acids (.k.2), and capable of producing 100 mg of peptide at 75% or greater purity in a single run (.k.3). Items controls under item paragraph .k would retain reasons for control that apply to the entire ECCN, which are proliferation of chemical and biological weapons (CB) column 2 and anti-terrorism (AT) column 1.

### **Request for Comments**

Consistent with section 1758 of ECRA, BIS welcomes comments on the following proposed control text for automated peptide synthesizers.

### **Export Control Reform Act of 2018**

On August 13, 2018, the President signed into law the John S. McCain National Defense Authorization Act for Fiscal Year 2019, which included the Export Control

Reform Act of 2018 (ECRA), 50 U.S.C. 4801–4852. ECRA provides the legal basis for BIS’s principal authorities and serves as the authority under which BIS issues this proposed rule.

### **Rulemaking Requirements**

1. Executive Orders 13563 and 12866 direct agencies to assess all costs and benefits of available regulatory alternatives and, if regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety effects, distribute impacts, and equity).

Executive Order 13563 emphasizes the importance of quantifying both costs and benefits, of reducing costs, of harmonizing rules, and of promoting flexibility. This proposed rule has been determined to be significant under Executive Order 12866.

2. Notwithstanding any other provision of law, no person may be required to respond to or be subject to a penalty for failure to comply with a collection of information, subject to the requirements of the Paperwork Reduction Act of 1995 (44 U.S.C. 3501 et seq.)

(PRA), unless that collection of information displays a currently valid Office of Management and Budget (OMB) Control Number. This regulation involves a collection currently approved by OMB under control number 0694-0088, Simplified Network Application Processing System. This collection includes, among other things, license applications, and carries a burden estimate of 29.4 minutes for a manual or electronic submission for a total burden estimate of 31,919 hours. BIS does not expect the burden hours associated with this collection to change. BIS estimates an increase by about 40 new licenses for these items each year, within the bounds of existing estimates.

Additional information regarding these collections of information – including all background materials -- can be found at <https://www.reginfo.gov/public/do/PRAMain> by using the search function to enter either the title of the collection or the OMB Control Number.

3. This proposed rule does not contain policies with federalism implications as that term is defined under Executive Order 13132.

4. Pursuant to section 1762 of the Export Control Reform Act of 2018 (ECRA) (50 U.S.C. 4821), this action is exempt from the Administrative Procedure Act (APA) (5 U.S.C. 553) requirements for notice of proposed rulemaking, opportunity for public participation and delay in effective date. However, BIS believes this proposed rule would benefit from public comment prior to issuance. Consistent with the Regulatory Flexibility Act, as amended by the Small Business Regulatory Enforcement Fairness Act of 1996 (SBREFA) (5 U.S.C. 601 *et seq.*), BIS has prepared the following initial regulatory flexibility analysis (IRFA) of the impact that this proposed rule, if adopted, would have on small businesses.

*Description of the Reasons Why Action Is Being Considered*

The policy reasons for issuing this proposed rule are discussed in the background section of the preamble of this document and, consequently, are not repeated here.

*Statement of the Objectives of, and Legal Basis for, the Proposed Rule; Identification of All Relevant Federal Rules Which May Duplicate, Overlap or Conflict with the Proposed Rule*

The objective of this proposed rule, and all other Section 1758 technology proposed rules published by BIS, is to control emerging and foundational technologies identified by BIS and its interagency partners as being essential to U.S. national security. The legal basis for this proposed rule is as follows: 50 U.S.C. 4801-4852.

No other Federal rules duplicate, overlap, or conflict with this proposed rule.

*Number and Description of Small Entities Regulated by the Proposed Action*

This proposed rule would apply to all persons engaged in the export, reexport or transfer (in-country) of the automated peptide synthesizers proposed for control under ECCN 2B352 and the related “technology” subject to the EAR. Presently, these

instruments and related “technology” are used in research and development activities in the biotechnology field (e.g., U.S. university, military and industrial laboratories).

Therefore, BIS anticipates that the proposed controls would result in ‘deemed’ export license applications (for the release of “technology” to foreign nationals located within the United States) to allow access to this “technology” by foreign students and faculty at U.S. universities, as well as by non-U.S. employees of U.S. biochemical firms. There would most likely also be ‘deemed’ reexport license applications for the release of this “technology” to third-country foreign nationals located in foreign countries who are engaged in research and development activities involving this “technology.”

BIS does not collect or maintain the data necessary to determine how many of the affected persons are small entities as that term is used by the Small Business Administration. Prior to issuing this proposed rule, BIS received 36 comments on biotechnology in response to its November 19 ANPRM, five of which were specific to this technology. None of these commenters specifically identified themselves as small businesses, although small businesses may have chosen to provide input through larger entities, such as trade associations.

However, BIS was able to estimate the number of license applications that the agency anticipates receiving as a result of this proposed rule and is using that estimate as a means of assessing the impact on small businesses. Using the North American Industry Classification System Codes (NAICS) 541714 (Research and Technology in Biotechnology (except Nanobiotechnology)), BIS determined that the standard small business size in this industry is 1,000 employees. Using Table 1a of the Census Bureau’s 2019 Exports by Company Type and Employment Size and extrapolating to 1,000 employees, BIS then estimated that approximately 40% of all identified companies that export in this industry are small businesses. BIS also estimates that it will receive 40 license applications per year for the items described in this proposed rule (see the PRA

estimates described in Rulemaking Requirements #2, above). Based on that information, BIS estimates that the agency will receive approximately 16 license applications per year from small businesses, or roughly 40% of the 40 estimated license applications.

In addition, based on the burden estimate for OMB under control numbers 0694-0088 (Simplified Network Application Processing System) and 0694-0096 (Five Year Records Retention Period), BIS expects that the total burden hours for small businesses associated with these EAR-related collections would increase only slightly, by just under 3 hours and 4 minutes (i.e., 6 applications  $\times$  30.6 minutes per response), for a total estimated cost increase of just under \$92 (i.e., 3 hours and 4 minutes  $\times$  \$30 per hour).

The amendments proposed in this rule, if implemented, also would trigger a small information collection burden under the U.S. Census Bureau's Foreign Trade Regulations (FTR) (15 CFR part 30), which contain the Electronic Export Information (EEI) filing requirements under the Automated Export System (AES). This FTR-related information collection has been approved by OMB under control number 0607-0152 (Automated Export System (AES) Program) and carries a burden hour estimate of 3 minutes per electronic submission. This collection, together with the aforementioned EAR-related information collections, would result in a total estimated cost increase to small businesses of just under \$94 (i.e., 3 hours and 7 minutes  $\times$  \$30 per hour). Note that, for purposes of consistency, the \$30 per hour cost estimate used for the EAR-related information collections described above is also applied to this FTR-related information collection (which also would involve work performed by export compliance specialists).

Based on the analysis provided above, the amendments proposed in this rule would not impose a significant economic impact on a substantial number of small businesses.

*Description of the Projected Reporting, Recordkeeping, and Other Compliance Requirements of the Proposed Rule*

The changes proposed in this rule, if adopted, would mean that certain items currently eligible for export, reexport or transfer (in-country) to most destinations under the No License Required (NLR) designation would require an EAR authorization (i.e., in accordance with the terms and conditions of an EAR license exception or a license issued by BIS). Adding these items to the CCL, to be controlled under ECCN 2B352, may also change the export clearance requirements under the FTR for certain exports of these items by triggering an EEI filing requirement in AES (note that the requirement generally does not apply to items below a certain value that are classified as EAR99, i.e., subject to the EAR, but not listed under an ECCN on the CCL).

To the extent that compliance with the changes proposed in this rule would impose a burden on persons, including small businesses, BIS believes the burden would be minimal. The reclassification process would need to be done only once per license applicant for exports, reexports or transfers (in-country) of these emerging technology items and, consequently, would constitute a one-time burden for each applicant. Similarly, assessing the availability of license exceptions and/or applying for and using BIS licenses would impose some minimal burden on persons, including small businesses.

However, it should be noted that these EAR requirements would likely have less impact than might otherwise be the case, because of the resources that BIS makes available to all exporters, including small businesses. Specifically, BIS's website has free on-line training explaining export basics, including instructions on how to register for and use BIS's online license application tool, and tips on how to complete a license application for chemical and biological items. BIS also provides free export counseling by telephone and e-mail via both its Washington, DC and Western Regional offices. In addition, BIS accepts requests for commodity classifications and processes them without charge to assist those exporters who need assistance in classifying their items for the purpose of determining whether any CCL-based license requirements would apply.

### *Significant Alternatives and Underlying Analysis*

As noted above, BIS does not believe that the amendments proposed in this rule, if published in a final rule, would have a significant economic impact on small businesses. Nevertheless, consistent with 5 U.S.C. 603(c), BIS considered significant alternatives to these proposed amendments to assess whether the alternatives would: (1) accomplish the stated objectives of this proposed rule (consistent with the emerging technology requirements in ECRA); and (2) minimize any significant economic impact of this proposed rule on small entities. BIS could have proposed a much broader control on peptide synthesizers controlled under ECCN 2B352 that would have captured a greater number of such items. However, that option would have had a greater impact not only on small businesses, but also on research and development laboratories (both academic and corporate), which are involved in advancing these technologies. BIS has determined that proposing focused controls on the items detailed above is the least disruptive alternative for implementing export controls in a manner consistent with controlling technology that has been determined, through the Section 1758 technology interagency process authorized under ECRA, to be essential to U.S. national security.

BIS is not proposing different compliance or reporting requirements for small businesses. If a small business is subject to a compliance requirement for the export, reexport or transfer (in-country) of this equipment and related “technology,” then it would submit a license application using the same process as any other company (i.e., electronically via SNAP-R). The license application process is free of charge to all entities, including small businesses. In addition, as noted above, the resources and other compliance tools made available by BIS typically serve to lessen the impact of any EAR license requirements on small businesses.

Lastly, consistent with 5 U.S.C. 603(c), BIS assessed the use of performance standards rather than design standards and also considered whether an exemption for

small businesses was practical under the circumstances (i.e., within the context of the changes proposed in this rule).

This proposed rule does not contain an exemption for small businesses from this license requirement because BIS and its interagency partners are assessing whether these controls are essential to U.S. national security. Specifically, items proposed for control could be used for nefarious purposes and, as such, controlling these items on the CCL may be determined to be essential to U.S. national security pursuant to the interagency process for identifying emerging and foundational technologies that is described in section 1758(a) of ECRA (50 U.S.C. 4817(a)). An exemption for small businesses would undermine the effectiveness of these proposed controls.

### *Conclusion*

BIS has identified the items addressed in this proposed rule as a technology suitable for evaluation under section 1758 of ECRA that warrants public notice and comment. Consequently, consistent with the Regulatory Flexibility Act, BIS has prepared this IRFA addressing the impact that this proposed rule, if adopted, would have on small entities. BIS's assessment indicates that the amendments proposed in this rule would not have a significant economic impact on a substantial number of small entities.

Please submit any comments concerning this IRFA in accordance with the instructions provided in the "ADDRESSES" section of this proposed rule.

### **List of Subjects in 15 CFR Part 774**

Exports, Reporting and recordkeeping requirements, Terrorism.

Accordingly, part 774 of the Export Administration Regulations (15 CFR parts 730-774) is proposed to be amended as follows:

### **PART 774 – THE COMMERCE CONTROL LIST**

1. The authority citation for part 774 continues to read as follows:

**Authority:** 50 U.S.C. 4801-4852; 50 U.S.C. 4601 et seq.; 50 U.S.C. 1701 et seq.; 10 U.S.C. 8720; 10 U.S.C. 8730(e); 22 U.S.C. 287c, 22 U.S.C. 3201 *et seq.*; 22 U.S.C. 6004; 42 U.S.C. 2139a; 15 U.S.C. 1824; 50 U.S.C. 4305; 22 U.S.C. 7201 *et seq.*; 22 U.S.C. 7210; E.O. 13026, 61 FR 58767, 3 CFR, 1996 Comp., p. 228; E.O. 13222, 66 FR 44025, 3 CFR, 2001 Comp., p. 783.

**Supplement No. 1 to part 774 – [Amended]**

2. Category 2 is amended by revising ECCN 2B352 to read as follows:

**Category 2 - Materials Processing**

**B. “Test”, “Inspection” and “Production Equipment”**

\* \* \* \* \*

**2B352 Equipment capable of use in handling biological materials, as follows (see List of Items Controlled).**

**License Requirements**

*Reason for Control:* CB, AT

<i>Control(s)</i>	<i>Country Chart (See Supp. No. 1 to part 738)</i>
CB applies to entire entry	CB Column 2
AT applies to entire entry	AT Column 1

**List Based License Exceptions** (See Part 740 for a description of all license exceptions)

*LVS:* N/A

*GBS:* N/A

**List of Items Controlled**

*Related Controls:* See ECCNs 1A004 and 1A995 for protective equipment that is not covered by this entry. Also see ECCN 9A120 for controls on certain “UAV” systems

designed or modified to dispense an aerosol and capable of carrying elements of a payload in the form of a particulate or liquid, other than fuel “parts” or “components” of such vehicles, of a volume greater than 20 liters.

*Related Definitions:* (1) “Lighter than air vehicles” – balloons and airships that rely on hot air or on lighter-than-air gases, such as helium or hydrogen, for their lift. (2) “UAVs” – Unmanned Aerial Vehicles. (3) ‘VMD’ – Volume Median Diameter.

*Items:*

a. Containment facilities and related equipment, as follows:

a.1. Complete containment facilities at P3 or P4 containment level.

***Technical Note to 2B352.a.1:*** *P3 or P4 (BL3, BL4, L3, L4) containment levels are as specified in the WHO Laboratory Biosafety Manual (3rd edition, Geneva, 2004).*

a.2. Equipment designed for fixed installation in containment facilities specified in paragraph a.1 of this ECCN, as follows:

a.2.a. Double-door pass-through decontamination autoclaves;

a.2.b. Breathing air suit decontamination showers;

a.2.c. Mechanical-seal or inflatable-seal walkthrough doors.

b. Fermenters and components as follows:

b.1. Fermenters capable of cultivation of micro-organisms or of live cells for the production of viruses or toxins, without the propagation of aerosols, having a total internal volume of 20 liters or greater.

b.2. Components designed for such fermenters, as follows:

b.2.a. Cultivation chambers designed to be sterilized or disinfected in situ;

b.2.b. Cultivation chamber holding devices; *or*

b.2.c. Process control units capable of simultaneously monitoring and controlling two or more fermentation system parameters (e.g., temperature, pH, nutrients, agitation, dissolved oxygen, air flow, foam control).

***Technical Notes to 2B352.b:***

***1. Fermenters include bioreactors (including single-use (disposable) bioreactors), chemostats and continuous-flow systems.***

***2. Cultivation chamber holding devices controlled by 2B352.b.2.b include single-use cultivation chambers with rigid walls.***

c. Centrifugal separators capable of the continuous separation of pathogenic microorganisms, without the propagation of aerosols, and having all of the following characteristics:

- c.1. One or more sealing joints within the steam containment area;
- c.2. A flow rate greater than 100 liters per hour;
- c.3. “Parts” or “components” of polished stainless steel or titanium; *and*
- c.4. Capable of in-situ steam sterilization in a closed state.

***Technical Note to 2B352.c: Centrifugal separators include decanters.***

d. Cross (tangential) flow filtration equipment and “accessories,” as follows:

d.1. Cross (tangential) flow filtration equipment capable of separation of microorganisms, viruses, toxins or cell cultures having all of the following characteristics:

- d.1.a. A total filtration area equal to or greater than 1 square meter (1 m<sup>2</sup>); *and*
- d.1.b. Having any of the following characteristics:
  - d.1.b.1. Capable of being sterilized or disinfected in-situ; *or*
  - d.1.b.2. Using disposable or single-use filtration “parts” or “components”.

***N.B.: 2B352.d.1 does not control reverse osmosis and hemodialysis equipment, as specified by the manufacturer.***

d.2. Cross (tangential) flow filtration “parts” or “components” (e.g., modules, elements, cassettes, cartridges, units or plates) with filtration area equal to or greater than 0.2 square meters (0.2 m<sup>2</sup>) for each “part” or “component” and designed for use in cross

(tangential) flow filtration equipment controlled by 2B352.d.1.

**Technical Note:** *In this ECCN, “sterilized” denotes the elimination of all viable microbes from the equipment through the use of either physical (e.g., steam) or chemical agents. “Disinfected” denotes a process to reduce the number of microorganisms, but not usually of bacterial spores, through the use of chemical agents, without necessarily killing or removing all organisms.*

e. Steam, gas or vapor sterilizable freeze-drying equipment with a condenser capacity of 10 kg of ice or greater in 24 hours (10 liters of water or greater in 24 hours) and less than 1000 kg of ice in 24 hours (less than 1,000 liters of water in 24 hours).

f. Spray-drying equipment capable of drying toxins or pathogenic microorganisms having all of the following characteristics:

f.1. A water evaporation capacity of  $\geq 0.4$  kg/h and  $\leq 400$  kg/h;

f.2. The ability to generate a typical mean product particle size of  $\leq 10$  micrometers with existing fittings or by minimal modification of the spray-dryer with atomization nozzles enabling generation of the required particle size; and

f.3. Capable of being sterilized or disinfected in situ.

g. Protective and containment equipment, as follows:

g.1. Protective full or half suits, or hoods dependent upon a tethered external air supply and operating under positive pressure;

**Technical Note to 2B352.g.1:** *2B352.g.1 does not control suits designed to be worn with self-contained breathing apparatus.*

g.2. Biocontainment chambers, isolators, or biological safety cabinets having all of the following characteristics, for normal operation:

g.2.a. Fully enclosed workspace where the operator is separated from the work by a physical barrier;

g.2.b. Able to operate at negative pressure;

g.2.c. Means to safely manipulate items in the workspace; and

g.2.d. Supply and exhaust air to and from the workspace is high-efficiency particulate air (HEPA) filtered.

**Note 1 to 2B352.g.2:** 2B352.g.2 controls class III biosafety cabinets, as specified in the WHO Laboratory Biosafety Manual (3rd edition, Geneva, 2004) or constructed in accordance with national standards, regulations or guidance.

**Note 2 to 2B352.g.2:** 2B352.g.2 controls any isolator having all of the characteristics described in 2B352.g.2.a through g.2.d, regardless of its intended use and its designation, except for medical isolators “specially designed” for barrier nursing or transportation of infected patients.

h. Aerosol inhalation equipment designed for aerosol challenge testing with microorganisms, viruses or toxins, as follows:

h.1. Whole-body exposure chambers having a capacity of 1 cubic meter or greater;

h.2. Nose-only exposure apparatus utilizing directed aerosol flow and having a capacity for the exposure of 12 or more rodents, or two or more animals other than rodents, and closed animal restraint tubes designed for use with such apparatus.

i. Spraying or fogging systems and “parts” and “components” therefor, as follows:

i.1. Complete spraying or fogging systems, “specially designed” or modified for fitting to aircraft, “lighter than air vehicles,” or “UAVs,” capable of delivering, from a liquid suspension, an initial droplet “VMD” of less than 50 microns at a flow rate of greater than 2 liters per minute;

i.2. Spray booms or arrays of ‘aerosol generating units’, “specially designed” or modified for fitting to “aircraft,” “lighter than air vehicles,” or “UAVs,” capable of delivering, from a liquid suspension, an initial droplet “VMD” of less than 50 microns at a flow rate of greater than 2 liters per minute;

i.3. ‘Aerosol generating units’ “specially designed” for fitting to the systems as

specified in paragraphs i.1 and i.2 of this ECCN.

***Technical Notes to 2B352.i:***

*1. Aerosol generating units are devices “specially designed” or modified for fitting to aircraft and include nozzles, rotary drum atomizers and similar devices.*

*2. This ECCN does not control spraying or fogging systems, “parts” and “components,” as specified in 2B352.i, that are demonstrated not to be capable of delivering biological agents in the form of infectious aerosols.*

*3. Droplet size for spray equipment or nozzles “specially designed” for use on aircraft or “UAVs” should be measured using either of the following methods (pending the adoption of internationally accepted standards):*

*a. Doppler laser method*

*b. Forward laser diffraction method.*

j. Nucleic acid assemblers and synthesizers that are both:

j.1 Partly or entirely automated; *and*

j.2. Designed to generate continuous nucleic acids greater than 1.5 kilobases in length with error rates less than 5% in a single run.

k. Peptide synthesizers that are:

k.1 Partly or entirely automated;

k.2 Capable of generating continuous peptide sequences greater than 75 amino acids;  
*and*

k.3 Capable of producing 100 mg of peptide at 75% or greater purity in a single run.

\* \* \* \* \*

**Matthew S. Borman,**

*Deputy Assistant Secretary for Export Administration.*